REMARKS

Claims 40-47 are pending in this application. Claim 40 has been amended to further describe the monoclonal antibody used in the method of the invention. The amendment to claim 40 is completely supported by the application as filed. In particular, support for amended claim 40 is found, *inter alia*, in applicants' specification at from page 33, line 5 to page 36, line 31. Thus there is no issue of new matter. Entry of this Amendment after Final Rejection is respectfully requested since it is believed to place the application in condition for allowance or, at a minimum, to materially reduce the issues for an appeal. Upon such entry, claims 40-47 as amended will be present in the application.

The Examiner stated in ¶3 of the Office Action that claims 40-47 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (citing *In re Rasmussen,* 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981) and *In re Wertheim,* 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976)). The Examiner stated that the claims include the limitations "specifically inhibit 67% or greater" and "inhibit 18% or less of fusion" which fail to receive adequate support in the disclosure.

Applicants respectfully traverse the Examiner's contention that the limitations "specifically inhibit 67% or greater" and "inhibit 18% or less of fusion" are not adequately supported in

their disclosure. Applicants contend that one skilled in the art, familiar with the practice of the art at the time of the filing date, could reasonably have found the invention as now claimed, i.e., with the above-described limitations, in the specification as filed. That is, as detailed below applicants' written disclosure of their invention is sufficiently clear that those skilled in the art would readily conclude that applicants made the invention having the limitations recited in the present claims at the time the application was filed. Thus the original application provides adequate support for fusion inhibition methods employing the claimed genus of monoclonal antibodies.

The Examiner stated that the disclosure describes the preparation, isolation, and preliminary characterization of four monoclonal antibodies produced by the hybridomas designated PA-3, -5, -6, and -7. The Examiner stated that applicants initially attempted to identify HIV-1 fusion inhibitory antibodies that did not bind specifically to CD4. The Examiner stated that immunization strategies employing HeLa and C8166 cell lines, as well as, proteinase-digested human erythrocytes were initially employed. The Examiner stated however, these strategies all failed to produce antibodies with the desired characteristics.

In response, applicants submit that applicants' initially unsuccessful attempts to produce antibodies with the desired characteristics, i.e., with the use of immunization strategies employing HeLa and C8166 cell lines, as well as proteinase-digested human erythrocytes, is wholly irrelevant to the issue of whether the subject claims limitations concerning the percentage of fusion inhibition are adequately supported in the written

disclosure. The experimental data which supports these claim limitations was obtained with the use of PM-1 cells as an immunogen. As acknowledged by the Examiner in the Office Action (see discussion following), the use of PM-1 cells as immunogens resulted in the identification of four hybridoma cell lines (PA-3, PA-5, PA-6 and PA-7) which produced antibodies having the desired fusion inhibition characteristics. Applicants submit that analysis of the fusion inhibition values obtained with the use of the subject antibodies for defining the ranges of fusion inhibition recited in applicants' claims is well within the skill of the ordinary artisan in this field. As discussed below, evidentiary support for the above argument is provided by the Declaration Under 37 C.F.R. §1.132 of Ronald C. Kennedy ("the Kennedy declaration") filed with applicants' response dated June 18, 2003 to the previous Office Action issued in this case.

The Examiner further stated in the Office Action that, finally, PM-1 cells were employed as an immunogen and four hybridoma cell lines were identified that produced antibodies with the desired characteristics (i.e., HIV-1 fusion inhibition without binding to CD4 or the viral Env). The Examiner stated that preliminary characterization of these antibodies suggests that PA-3 and PA-5 recognize CDlla or CD18, whereas, PA-6 and PA-7 recognize HLA Class II.

The Examiner then stated that the fusion inhibitory activities of these antibodies were further characterized in a HeLa-env RET assay wherein it was reported that PA-3, -5, -6, and -7 inhibited fusion between PM-1 cells and HeLa-env_{JR-FL}, 85%, 96%, 92% and 67%, respectively. The Examiner stated that fusion inhibitory studies involving HeLa-env_{LAI} cell lines provided

inhibitory values of 90%, 100%, 81% and 69% for said antibodies. The Examiner stated that Sup-T1 fusion inhibitory studies produced inhibitory rates of 2.5%, 0%, 18%, and 11%. The Examiner stated that thus, the skilled artisan would reasonably conclude that applicants were in possession of the monoclonal antibodies PA-3, -5, -6, and -7. **The Examiner then stated that appropriate inhibitory methodology claim language employing these four Mabs would be acceptable.**

In response to the Examiner's statement that appropriate inhibitory methodology claim language employing the four Mabs PA-3, -5, -6 and -7 would be acceptable, applicants respectfully submit that claim 40 has been amended as indicated above such that it now recites that a monoclonal antibody used in the method of the invention must be at least as active as monoclonal antibody PA-7 in inhibiting fusion and less active than antibody PA-6 in inhibiting such fusion. Applicants' claims thus now further define the genus of antibodies for use in the claimed method in terms of the characteristics of several of the antibodies characterized as working examples in applicants' specification.

The Examiner is attempting to limit applicants' claims to the specific antibodies actually reduced to practice. This has never been the law for any genus claim and it should not be a special rule just for antibodies. Rather, the Court of Appeals for the Federal Circuit held in *Lilly* that written description of a genus may be satisfied by having possession of a representative number of species falling within the scope of that genus (*Regents of Univ. of Cal. V. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997)).

The *Enzo* court said much the same:

Although one may envision a general concept, what one usually does first in making or isolating a chemical or chemical-related invention is to obtain a specific material or materials. One then broadens the concept to extend it as far as one envisions that other materials will have the same utility and can be similarly made. That broadened concept becomes the genus in a patent application that is both the broadest statement constituting a written description and usually claim 1. One then elaborates to fill in the genus with representative examples of compounds or substances that fall within the genus. That is part of the written description needed to support the generic claim. *Enzo Biochem. Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 974 (Fed. Cir. 2002).

Thus, a requirement to limit the claims to the specific antibodies disclosed (i.e., PA-3, PA-5, PA-6 and PA-7) ignores these precedents of the written description required to support a genus. Instead, as discussed below the Examiner appears to focus on whether the structure of the antibodies within the genus is provided in applicants' written disclosure of the invention. This is contrary to *Lilly*. There, the Federal Circuit stated that the written description of a genus was satisfied by common structure or by a representative number of examples:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus **or of a recitation of structural features common to members of the genus which features constitute a substantial portion of the genus** (emphasis supplied). (*Lilly*, 119 F.3d at 1569).

The PTO Written Description Guidelines similarly recognize that written description can be satisfied by a representative number of examples **or** by structure:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice . . . **or by disclosure of relevant identifying characteristics, i.e., ~~structure or other physical and/or chemical properties~~** (emphasis supplied). (66 Fed. Reg. 1099 at p. 11 (2001).

Applicants submit that they have met the requirements regarding the written description of their invention as claimed in that the antibodies used in the subject method are described in claim 40 in terms of "physical and/or chemical properties" (i.e., their fusion inhibition capabilities) common to the claimed genus with specific reference to the properties of the antibodies generated as working examples. For the reasons above, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 40-47 under 35 U.S.C. §112, first paragraph.

The scope of applicants' disclosure, moreover, goes far beyond providing the working examples of antibodies useful in the method of the invention. As indicated below the teachings of the specification, when coupled with the general knowledge in the field about making monoclonal antibodies as of the January 17, 1996 effective filing date of this application, would readily permit one of ordinary skill in this art to produce and use an antibody in accordance with the method now claimed.

As pointed out, for example, in ¶ 7 of the Kennedy declaration, it was standard practice as of January 17, 1996 for one skilled in this art to make a monoclonal antibody by immunizing a mouse with a particular immunogen. Moreover, monoclonal technology, according to the Dr. Kennedy, is a technology that was widely used and highly predictable as of January 17, 1996.

Dr. Kennedy stated further in ¶9 of his declaration that, based on the disclosure contained in applicants' specification, coupled with the general knowledge in the field about making monoclonal antibodies as of January 17, 1996, one skilled in the art could have readily made a monoclonal antibody such as that recited for use in the claimed method. Further according to Dr. Kennedy, making monoclonal antibodies to cell surface markers on whole cells was a well-defined technology as of January 17, 1996. Dr. Kennedy additionally stated that as of January 17, 1996, the level of skill of one of ordinary skill in the art of making a monoclonal antibody was a laboratory technician with a bachelor's degree and one to two years of experience working with hybridomas. Further according to Dr. Kennedy, such a person of ordinary skill could have readily made a monoclonal antibody such as is recited in the claims for use in applicants' claimed method prior to January 17, 1996. In particular, the experimental details section of the application's specification teaches on pages 24-36 a straightforward, reproducible method for making and identifying such a monoclonal antibody.

The written description of the invention provides detailed guidance and direction for making a monoclonal antibody and selecting a monoclonal antibody having the chacteristics as recited in applicants' claims. As pointed out, for example, in ¶¶10-14 of the Kennedy declaration, the application describes, *inter alia*, the following:

a) a source of an immunogen for eliciting a monoclonal antibody for use in the method of the invention (PM-1 cells, page 33, lines 9-11);

b) a method for obtaining a monoclonal antibody by recovering supernatant from hybridomas generated by immunizing mice with PM-1 cells (page 24);

c) a screening assay called the resonance energy transfer ("RET") assay for identifying a monoclonal antibody having the ability to inhibit HIV-1 envelope glycoprotein mediated membrane fusion (pages 25-26);

d) adaptations to the RET screening assay such that HeLa cells expressing envelope glycoprotein from HIV-1_{JR-FL} ("HeLa-env_{JR-FL} cells") and HeLa cells expressing envelope glycoprotein from HIV-1_{LAI} ("HeLa-env_{LAI} cells") may be used for differential screening (page 25) for monoclonal antibodies having the characteristics as recited in the claims for antibodies which will function in accordance with the method recited in applicants' claims.

e) Monoclonal antibodies generated by immunizing mice with CD4+ PM-1 cells which inhibit fusion between HeLa-env_{JR-FL} and CD4+ PM-1 cells; the identification and selection of monoclonal antibodies that fit the characteristics of inhibiting fusion between CD4+ PM-1 cells and HeLa-env_{JR-FL} cells by at least 67% and only inhibiting fusion between CD4+SUP-T1 cells and HeLa-env_{LAI} cells by at most 18% (Table 1 on page 34).

f) Additional methods are provided for further characterization of the fusion-inhibiting monoclonal antibodies for use with the method of the present invention. These methods, which are described at pages 26-30 and 34-34 of applicants' specification, demonstrate that the fusion-inhibiting monoclonal antibodies for use in the claimed method react with an antigen on the surface of a PM-1 cell, do not react with

HIV-1 envelope glycoprotein or CD4, and do not cross-react with an antigen on the surface of a SUP-T1 cell.

g) The application describes specific examples of monoclonal antibodies made using the above-described methodology which are useful in the method of the invention in Table 1 on page 34. As noted above, independent claim 40 has been amended to recite that the antibody used in the invention is at least as active as monoclonal antibody PA-7 in inhibiting fusion and less active than monoclonal antibody PA-6 in inhibiting fusion.

In ¶11 of his declaration Dr. Kennedy additionally stated that it is not necessary for one of ordinary skill in the art to know the antigenic determinants or epitopes on the whole cells used for immunization, or their structural configuration in order to make and successfully identify a monoclonal antibody having the fusion-inhibition characteristics required to practice the method of the invention. Further according to the declarant, it is well-established that having a starting immunogenic source such as an immunogenic whole cell and following an immunization method, a series of monoclonal antibodies will be elicited and that the screening method taught in the application allows one skilled in the art to identify and select monoclonal antibodies which, in accordance with the methods recited in claim 40, when contacted with a CD4+ cell, will (a) specifically inhibit 67% or greater of fusion of a CD4+ PM-1 cell to a HeLa cell expressing envelope glycoprotein from HIV-1_{JR-FL} , and (b) inhibits 18% or less of fusion of a CD4+ SUP-T1 cell to a HeLa cell expressing envelope protein from HIV-1_{LAI}, wherein the antibody (i) does not cross-react with HIV-1 envelope glycoprotein or CD4, (ii) reacts with

an antigen on the surface of a PM-1 cell, and (iii) does not react with an antigen on the surface of a SUP-T1 cell, so as to thereby inhibit HIV-1 infection of the CD4+ cell.

Dr. Kennedy additionally stated, in ¶12 of his declaration, that various immunogenic whole cells, such as PM-1 cells, HeLa cells, C8166 cells and protease digested human erythrocytes, were used to generate monoclonal antibodies. One of the immunogenic whole cells, i.e., PM-1 cells, resulted in eliciting antibodies that blocked fusion of CD4+ PM-1 cells to HeLa-env_{JR-FL} cells, as identified by the screening methods. Thus according to the declarant, the specification unequivocally shows that PM-1 cells or analogous cells may be successfully used as an immunogen to make an HIV-1 fusion-blocking antibody as disclosed in the specification for use in the method recited in the claims.

Accordingly, therefore, applicants respectfully submit that one skilled in this art, familiar with the practice of the art on the filing date, would reasonably have found in the specification as filed teachings of how to make, select and characterize monoclonal antibodies with the characteristics recited in claims 40-47. Applicants' disclosure is sufficiently clear that one of ordinary skill in this art would have concluded that applicants were in possession of monoclonal antibodies having the currently claimed binding characteristics and that the application thus provides adequate support for fusion inhibitory methods employing the presently claimed monoclonal antibodies.

The Examiner further stated in the Office Action that Applicants are reminded that the essence of the statutory requirement governing written description is whether one skilled in the art,

familiar with the practice of the art at the time of the filing date, could reasonably have found the later claimed invention in the specification as filed (citing *In re Kaslow,* 707 F.2d 1366, 1375, 217 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983), *In re Wilder,* 736 F.2d 1516, 1520 222 U.S.P.Q. 349, 372 (Fed. Cir. 1984, *cert, denied,* 469 U.S. 1209 (1985)and *Texas Instruments, Inc.* v. *International Trade Comm'n,* 871 F.2d 1054, 1063, 10 U.S.P.Q.2d 1257, 1263 (Fed. Cir. 1989)). The Examiner stated that moreover, the courts have stated that the evaluation of written description is highly fact-specific, and that broadly articulated rules are inappropriate (citing *In re Wertheim,* 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976)and *In re Driscoll,* 562 F.2d 1245, 1250, 195 U.S.P.Q. 434, 438 (C.C.P.A. 1977)). The Examiner stated that it is also important to remember that the true issue in question is not whether the specification enables one of ordinary skill in the art to make the later claimed invention, but whether or not the disclosure is sufficiently clear that those skilled in the art will conclude that the applicant made the invention having the specific claim limitations (citing *Martin* v. *Mayer,* 823 F.2d 500, 505, 3 U.S.P.Q.2d 1333, 1337 (Fed. Cir. 1987)).

In response, applicants submit that the specification clearly discloses the invention recited in amended claim 40 for the reasons set forth above, and that this contention is supported by Dr. Kennedy's declaration, which is entitled to evidentiary weight under 37 C.F.R., §1.132. The claims thus recite an invention which one of ordinary skill in this art, familiar with the practice of the art at the time of the effective filing date of the application, would reasonably have found described in the specification as filed.

Applicants thus respectfully traverse the Examiner's statement on page 3 of the Office Action that, upon perusal of the disclosure, the skilled artisan would not conclude that applicants were in possession of monoclonal antibodies with the currently claimed binding characteristics. The Examiner stated that the claims are currently directed toward a large genus of antibodies that were neither contemplated nor described by the applicants. The Examiner stated that while a small number of antibodies have been identified and partially characterized, at no time did applicants contemplate making and using antibodies with the specifically recited binding characteristics. Further in support of his position, the Examiner stated that there is no description of attempting to isolate and purify antibodies with specific inhibitory ranges of 67% or greater in PM-1 cell lines or 18% or less in Sup-T1 cell lines. The Examiner stated that the courts have also concluded that the disclosure of a single or limited number of species is insufficient support for claims directed toward a broader genus (citing *In re Gosteli,* 872 F.2d 1008, 1010, 10 U.S.P.Q.2d 1614, 1616 (Fed. Cir. 1989), *In re Blaser,* 556 F.2d 534, 538-39, 194 U.S.P.Q. 122, 125-26 (C.C.P.A. 1977), *In re Wertheim,* 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976) and In *re Lukach,* 442 F.2d 967, 969, 169 U.S.P.Q. 795, 797 (C.C.P.A. 1971)). The Examiner stated that thus, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing.

In response, however, further to their arguments above applicants submit that there is no requirement that they describe attempting to achieve that which they in fact did achieve and now

accordingly claim as their invention. That is, as reported in their specification, applicants produced, screened and identified a number of monoclonal antibodies having inhibitory values within the ranges recited in claim 40. Moreover, as indicated above, the specification teaches one of ordinary skill how to produce, screen and identify antibodies which fall within the inhibitory ranges recited in the claims. Based on these teachings, coupled with the level of ordinary skill in this art at the time the application was filed, as stated, e.g., in ¶9 of the Kennedy declaration, "[o]ne skilled in the art could have readily made a monoclonal antibody having the fusion inhibition characteristics recited in . . . . [applicants' claims]." Moreover, as noted above, applicants' independent claim has been amended such that it now specifically recites that genus of monoclonal antibodies useful in the invention are those which are at least as active as monoclonal antibody PA-7 (provided as a working example) and less active than monoclonal antibody PA-6 (another working example). Applicants submit, therefore, that a skilled artisan would reasonably conclude that applicants were in possession of the invention as presently claimed at the time the application was filed.

The Examiner additionally stated in the Office Action that Applicants had traversed the rejection and argued that sufficient support exists for the claimed invention. The Examiner stated that a declaration was also provided by Dr. Ronald C. Kennedy as further support. The Examiner stated that neither the arguments or declaration are sufficient to overcome the rejection. The Examiner stated that nothing contained in the response directs the skilled artisan to a specific passage or portion of the disclosure that clearly and unambiguously describes the claimed

invention. The Examiner stated that accordingly the rejection is properly maintained.

Applicants submit, however, that the manner of the Examiner's response to the declaration submitted by Dr. Kennedy does not meet the requirements set forth by the Federal Circuit's decision in *In re Alton, 76 F.3d 1168* which deals, *inter alia*, with the requirements for responding to such declarations by an Examiner. In *Alton*, the applicant had provided an evidentiary declaration of one skilled in the art under 37 C.F.R. 1.132 ("the Wall declaration") to support his contention that the specification of the application contained a sufficient written description of the claimed invention. The Examiner, and later the Board of Appeals, gave no weight to the declaration, characterizing it (at p. 1171) as being "[a]n opinion affidavit on the ultimate legal question at issue" and thus provided no rebuttal to the points raised in the declaration.

The Federal Circuit, however, held that the Examiner had erred in summarily dismissing the declaration without an adequate explanation of why the declaration failed to rebut the *prima facie* case of inadequate description.

Applicants submit, therefore, that the Examiner is required to rely upon more than just his opinion in traversing the points raised by Dr. Kennedy in his declaration. That is, the Examiner must point to some tangible source, i.e., a patent, treatise, journal article, etc. to "disprove" the contentions set forth in the declaration. Applicants contend that the Examiner has not met this burden and thus has not overcome the declaration.

Further to the above, in the context of declarations submitted under 1.132 to establish enablement, M.P.E.P. §2164.05 states:

> The examiner must . . . weigh all the evidence before him . . ., including the specification and any new evidence supplied by the applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled. The examiner should never make the determination based on personal opinion. The determination should always be based on the weight of all of the evidence (emphasis in original).

Applicants submit, however, that the Examiner has relied in the present instance on his own opinion of how matters stand in the art to counter the points raised in the Kennedy declaration. He has not, as required, provide any evidence to support his arguments concerning the validity of the statements made by Dr. Kennedy. Applicants therefore respectfully submit that the Examiner has not carried his burden of overcoming the evidence provided by Dr. Kennedy's declaration which, when taken in conjunction with the claim amendments and arguments submitted herewith, completely supports applicants' contention that the teachings in the present specification meet all of the requirements under 35 U.S.C. §112, first paragraph, for providing an appropriate written description of the presently claimed invention.

The Examiner additionally stated in ¶4 of the Office Action that claims 40-47 stand further rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (citing In re Rasmussen, 650 F.2d 1212, 211 U.S.P.Q. 323

(C.C.P.A. 1981)and In re Wertheim, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976)). The Examiner stated that to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention (citing Vas-Cath, Inc., v. Mahurkar, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116). In response, applicants contend that the claim amendments and arguments provided above clearly demonstrate that the written description of their invention meets this requirement.

The Examiner stated that the issue raised in this application is whether the original application provides adequate support for fusion inhibitory methods employing the broadly claimed genus of monoclonal antibodies (emphasis provided by applicants). Applicants respectfully submit, however, that the presently claimed fusion inhibitory methods employ a genus of monoclonal antibodies which is not "broadly claimed" as stated by the Examiner. A monoclonal antibody falling within the scope of, e.g., claim 40, must meet a number of very specific requirements as follows:

1) it must specifically inhibit 67% or greater of fusion of a CD4+ PM-1 cell to a HeLa cell expressing envelope glycoprotein from HIV-1_{JRFL};

2) it must inhibit 18% or less of fusion of a CD4+ SUP-T1 cell to a HeLa cell expressing envelope protein from HIV-1_{LAI};

3) it does not crossreact with HIV-1 envelope glycoprotein;

4) it does not crossreact with CD4;

5) it reacts with an antigen on the surface of a PM-1 cell;

6) it does not react with an antigen on the surface of a SUP-T1 cell; and

7) it is at least as active as monoclonal antibody PA-7 in inhibiting fusion as recited in #1 above and less active than monoclonal antibody PA-6 in inhibiting fusion as recited in #2 above.

Applicants' specification clearly describes the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventors had possession thereof at the time the application was filed.

The Examiner stated that an applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1996 (Fed. Cir. 1997). As indicated above, applicants contend that they have met that burden. The Examiner further stated that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. Applicants note, however, the use of the modifier "may" in discussing the sufficiency of the description. The language quoted above from the Office Action thus indicates that at least in come instances,

i.e., as in the present case, a claimed invention could be described in terms of a method of its making coupled with its function.

Notwithstanding the above, however, applicants again draw the Examiner's attention to the language added to claim 40 which requires that the monoclonal antibody used in the method of the invention be at least as active as monoclonal antibody PA-7 in inhibiting fusion and and less active then monoclonal antibody PA-6 in inhibiting fusion. The antibodies for use in the method of the invention are clearly described in applicants' specification, together with methods for producing, screening and identifying these antibodies, and the Examiner is thus respectfully requested to reconsider and withdraw the rejection of the claims under §112, first paragraph.

The Examiner additionally stated in the Office Action that a biomolecule sequence described only by functional characteristics, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest (citing *In re Bell,* 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993)and *In re Deuel,* 51 F.3d 1552, 34 U.S.P.Q.2d 1210'(Fed. Cir. 1995)). The Examiner stated that a lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process (citing *Fujikawa v, Wattanasin,* 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed.

Cir. 1995)). The Examiner stated that the court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

The Examiner stated that an applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. The Examiner stated that an applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics [see, e.g., applicants' arguments above concerning the *Lilly* and *Enzo* cases, which are incorporated herein by reference] which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. The Examiner stated that for some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The Examiner stated that the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. The Examiner stated that without such a correlation, the capability to recognize or understand the structure from the mere recitation of function and minimal structure is highly unlikely. The Examiner stated that in the latter case, disclosure of function alone is little more than

a wish for possession; it does not satisfy the written description requirement(citing *Regents of the University of California v. Eli Lilly,* 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert, denied,* 523 U.S. 1089 (1998)and *In re Wilder,* 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 10 1984)). The Examiner stated that factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

In response, the Examiner's attention is once again respectfully directed to ¶11 of the Kennedy declaration. As noted above in the discussion of the Examiner's first ground of rejection under §112, Dr. Kennedy stated therein that to prepare antibodies for use in practicing the claimed method it is NOT necessary for one skilled in the art to know the antigenic determinants or epitopes on the whole cells used for immunization or their structural configuration. Dr. Kennedy further stated that it is well-established that having a starting immunogenic source such as an immunogenic whole cell and following an immunization method, a series of monoclonal antibodies will be elicited. Dr. Kennedy additionally stated that it is also well established that the screening method [provided in applicants' specification] allows one skilled in the art to identify and select monoclonal antibodies which, when contacted with a CD4+ cell in accordance with the claimed method, will (a) specifically inhibit 67% or greater of fusion of a CD4+PM-1 cell to a HeLa cell expressing envelope glycoprotein from HIV-1_{JR-FL}, and (b) inhibit 18% or less

of fusion of a CD4+ SUP-T1 cell to a HeLa cell expressing envelope protein from HIV-1_{LAI}, wherein the antibody (i) does not cross-react with HIV-1 envelope glycoprotein or CD4, (ii) reacts with an antigen on the surface of a PM-1 cell, and (iii) does not react with an antigen on the surface of a SUP-T1 cell.

As additionally stated by Dr. Kennedy in ¶13 of his declaration, the data included in Table 1 on page 34 clearly demonstrates that the PA-3, PA-5, PA-6 and PA-7 monoclonal antibodies disclosed by applicants and specifically taught for use in the method of the invention are capable, as also recited in the subject claims, of specifically inhibiting 67% or greater of fusion of a CD4+PM-1 cell to a HeLa cell expressing envelope protein from HIV-1_{JR-FL} and inhibiting 18% or less of fusion of a CD4 SUP-T1 cell to a HeLa cell expressing envelope protein from HIV-1_{LAI}. The amended language of claim 40 results in an even closer correspondence between how the invention is recited in the present claims and how it is disclosed in applicants' written description.

The Examiner stated that in the instant application, the disclosure provides generic methods for obtaining antibodies that are capable of inhibiting HIV-1 envelope-mediated cell fusion. The Examiner stated that however, these screening procedures are not designed to identify Mabs with the currently claimed binding characteristics. The Examiner stated that they are simply designed to identify fusion inhibitors. The Examiner stated that, moreover, the disclosure fails to provide any detailed guidance pertaining to the structural characteristics of the monoclonal antibodies employed in the fusion assay. The Examiner stated that applicants have failed to provide any guidance pertaining to the amino acid sequence of any of

the given antibodies. The Examiner stated that applicants have failed to provide any detailed structural guidance pertaining to the antigenic determinants that are recognized by said antibodies. The Examiner stated that thus, the disclosure fails to provide even a modicum of structural information pertaining to the antibodies of interest. The Examiner stated that moreover, the disclosure does not provide a reproducible method for making antibodies with the claimed binding characteristics. The Examiner stated that four antibodies were identified using the claimed method and they all had different binding characteristics. The Examiner stated that these findings are not unexpected given the unpredictability of the art. The Examiner stated that accordingly, the skilled artisan would reasonably conclude that applicants have failed to provide an adequate written description for the claimed genus of antibodies employed in the claimed methodology.

With respect to the Examiner's statement above that applicants' screening procedures are not designed to identify Mabs with the currently claimed binding characteristics, applicants respectfully submit that their claims are not directed to the method(s) by which the antibodies are produced, isolated and/or characterized. Rather, the present claims are directed to a method of inhibiting HIV-1 infection of a CD4+ cell using antibodies with certain specific well-described characteristics. Thus the purpose behind applicants' screening methods is moot and of no consequence to the issue under consideration.

As to the statements noted above concerning the lack of disclosure relating to the structure of the claimed antibodies, the Examiner's attention is respectfully directed to ¶15 of the

Kennedy declaration which states that for one skilled in the art to practice the method of the invention as recited, for example, in claim 40, such individual need not know the structure of the antibody molecules which operate in accordance with the method. Dr. Kennedy then further stated that it is the function of these molecules, as defined by the above-described fusion-inhibition characteristics, which is the factor that controls the selection of the appropriate antibodies (emphasis supplied by applicants). This view is, moreover, completely supported by the holdings in the *Lilly* and *Enzo* cases discussed above by applicants

The Examiner next stated that applicants argued that a sufficient written description of the claimed genus of compounds was present. The Examiner stated that a declaration was provided by Dr. Ronald C. Kennedy further asserting that a sufficient written description for the claimed invention was present. The Examiner stated that these arguments are insufficient. The Examiner stated that the disclosure provides a generic method for obtaining monoclonal antibodies with fusion inhibitory properties. The Examiner stated that however, the disclosure fails to set forth any of the molecular determinants responsible for the antiviral activities of the required Mabs. The Examiner stated that the disclosure fails to set forth the antigenic determinants recognized by the Mabs of interest. The Examiner stated that thus, the applicants have no knowledge of the amino acid sequences that are critical for the recited antiviral activities. The Examiner stated that thus, this situation is quite apropos to the case law cited above wherein the courts have clearly concluded that a generic method of production without any further structural guidance is insufficient support for a broad genus of products.

In response, applicants reiterate their argument made above that the manner of the Examiner's response to Dr. Kennedy's declaration does not meet the legal requirements for overcoming the evidentiary weight to which such statements are entitled. The Examiner stated that Dr. Kennedy's arguments are "insufficient", but the Examiner does not, however, provide evidence of any sort which would contravene, for example, Dr. Kennedy's statements in ¶11 of his declaration to the effect that it is not necessary for one skilled in the art to know the antigenic determinants or epitopes present on the whole cells used for immunization, or their structural configuration. Nor does the Examiner point to anything which would disprove the statement in ¶15 of the declaration that for one skilled in this art to practice the claimed method, such individual need not know the structure of the antibody molecules which operate in accordance with the method. Rather, it is the function of these molecules, as defined by their fusion-inhibition characteristics, which is the factor that controls the selection of the appropriate antibodies.

Further, applicants additionally traverse the Examiner's statement that the present situation is "quite apropos" to the cited case law where the courts have concluded that a generic method of production without any further structural guidance is insufficient support for a broad genus of products. The Examiner is respectfully reminded that the present claims are not directed to "a broad genus of products." Rather, they are directed to a method of inhibiting HIV-1 infection of a CD4+ cells using antibodies with a number of specific and well-defined fusion inhibition characteristics.

Summary

For all of the reasons set forth hereinabove, applicants submit that the invention recited in claims 40-47 as amended and new claim 48 is described in the specification as filed in a manner which meets all of the requirements under 35 U.S.C. §112, first paragraph. The Examiner is thus respectfully requested to reconsider and withdraw the rejection of claims 40-47 under §112.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' invites the Examiner to telephone their attorneys at the number provided below.

A fee of $475.00 for a three-month extension of time is deemed necessary in connection with the filing of this response and a check for the indicated amount is enclosed. If any additional fee(s) is due, authorization is hereby given to charge the required fee to Deposit Account No. 03-3125.

Respectfully submitted,

Mark A. Farley

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Mark A. Farley 3-24-02

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